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Off-pump versus on-pump coronary artery bypass surgery in patients with actively treated diabetes and multivessel coronary disease.

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Abbreviations

AF: atrial fibrillation

BITA: bilateral internal thoracic artery

BMI: body mass index

CCS: Canadian Cardiovascular Society

CVA: cerebrovascular event

COPD: chronic obstructive pulmonary disease;

DM: diabetes

IR: incomplete revascularization

IABP intra-aortic balloon pump

LMD: left main disease

LVEF: left ventricular ejection fraction

MI: myocardial infarction

OPCAB: off-pump coronary artery bypass

ONCAB: on-pump coronary artery bypass

PCI: percutaneous coronary intervention

PVD: peripheral vascular disease

RRT: renal replacement therapy

sCr: serum creatinine

TVD: three vessel disease

PSM: propensity score matching

SDM: standardized mean difference

Central message

Off-pump bypass surgery is a safe and feasible option for diabetic patients with multivessel disease, it reduces the incidence of early complications and provides long term survival benefit similar to on-pump surgery

Perspective statement

Off-pump bypass surgery remains valid option for diabetic patients with multivessel disease as it reduces the incidence of early complications and provides long term survival benefit similar to on-pump surgery. Its use should not be discouraged in such a high risk subgroup.

Abstract

Objective(s): We conducted a single centre analysis on short-term outcomes and long term survival in actively treated diabetic patients undergoing off pump coronary artery bypass (OPCAB) versus on pump coronary artery bypass (OPCAB) surgery.

Methods: The final population consisted of 2450 patients with actively treated diabetes (mean age 66±9 years; F/M 545/1905, 22%). Of those, 1493 subjects were orally treated and 1011 were on insulin. OPCAB and ONCAB were performed in 1253 and 1197 patients respectively. Propensity score matching was used to compare the two matched groups.

Results: When compared to ONCAB, OPCAB was significantly associated with a significant risk reduction for postoperative cerebrovascular accident (OR 0.49; 95%CI 0.25-0.99; P=0.04), need for postoperative IABP (OR 0.48; 95%CI 0.30-0.77; P=0.002) and re-exploration for bleeding (OR 0.55; 95%CI 0.33-0.94; P=0.02). OPACB did not significantly affect early (HR 1.32; 95%CI 0.73-2.40; P=0.36) and late mortality (HR 1.08;95%CI 0.92-1.28; P=0.32). However, OPCAB with incomplete revascularization was associated with a reduced survival rate when compared to OPCAB with complete revascularization (HR 1.82; 95%CI 1.34-2.46; P=0.0002) and ONCAB with complete revascularization (HR 1.83; 95%CI1.36-2.47; P<0.0001).

Conclusions: OPCAB is a safe and feasible option for diabetic patients with multivessel disease, it reduces the incidence of early complications including postoperative cerebrovascular events and provides excellent long term survival similar to ONCAB surgery in case of complete revascularization.

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Diabetes mellitus (DM) is a major public health and economic problem with a dramatic increase in prevalence and incidence [1]. Coronary heart disease is highly prevalent and is the major cause of morbidity and mortality among diabetic patients [2]. Patients with DM account for approximately one quarter of all patients who undergo coronary revascularization procedures each year [3]. Coronary artery bypass graft (CABG) surgery when compared with percutaneous coronary intervention (PCI) has been shown to be associated with better outcomes in patients with diabetes [4], and current clinical guidelines recommend CABG as the preferred revascularization strategy in diabetic patients with complex coronary artery disease [5]. However, DM has a significant negative impact on the clinical outcome of coronary surgery in the long term as well as in the short term [6]. The debate on the effectiveness or otherwise of off pump coronary artery bypass (OPCAB) versus on pump coronary artery bypass (ONCAB) surgery continues [7-9]. In particular the role of OPCAB in the management of diabetic patients remains controversial as comparative data are scarce and inconclusive [10-13]. A recent sub-analysis of the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial [10] suggested that patients with diabetes had greater risk of major cardiovascular long-term events after OPCAB than after ONCAB. However, this study presented several limitations including very small sample size and definitive conclusions could not be drawn [14]. In this study, we used a large consecutive cohort with DM operated over a 20 years period at a single institution, to perform a propensity score matching (PSM) analysis of ONCAB versus OPCAB on short-term outcomes and long term survival.

Methods

The study was conducted in accordance with the principles of the Declaration of Helsinki. The local audit committee approved the study, and the requirement for

individual patient consent was waived. We retrospectively analysed prospectively collected data from The National Institute for Cardiovascular Outcomes Research (NICOR) NACSA registry for all isolated first time CABG procedures performed at the Bristol Heart Institute, Bristol United Kingdom from April 1996 to April 2015. Reproducible cleaning algorithms were applied to the database, which are regularly updated as required. Briefly, duplicate records and non-adult cardiac surgery entries were removed; transcriptional discrepancies harmonized; and clinical conflicts and extreme values corrected or removed. The data are returned regularly to the local units for validation.

Further details and definition of variables are available at http://www.ucl.ac.uk/nicor/audits/adultcardiac/datasets. Among 15119 isolated first time CABG cases performed during the study period, we selected subjects who met the following criteria: patient with actively treated DM at the time of surgery; multivessel coronary disease; data regarding the surgical strategy adopted (OPCAB versus ONCAB) was available. Patients with no diabetes (n=12439), single vessel disease (n=121) and no data regarding surgical strategy adopted (n=109) were excluded. The final population consisted of 2450 patients with actively treated diabetes (mean age 66±9 years; F/M 545/1905, 22%). Of those, 1493 subjects were orally treated and 1011 were on insulin. OPCAB and ONCAB were performed in 1253 and 1197 patients respectively (Figure 1). In the present series OPCAB was performed according to surgeon preference and not based on specific clinical indications (Video 1). Normothermic blood cardioplegia was the standard strategy for ONCAB cases during the study period. Blood glucose level was strictly maintained at less than 11.1 mmol/L perioperatively using insulin infusion and postoperatively for both OPCAB and ONCAB procedures.

Pre-treatment variables and study end-points

The effect of OPCAB over ONCAB was adjusted for the following variables including: age, gender, body mass index (BMI); previous myocardial infarction (MI) within 30 days, previous percutaneous coronary intervention (PCI); diabetes mellitus (DM) on insulin; chronic obstructive pulmonary disease (COPD); Canadian Cardiovascular Society (CCS) class III or IV; New York Heart Association (NYHA) class III or IV; current smoking; serum creatinine ≥200 mmol/l, previous cerebrovascular accident (CVA); peripheral vascular disease (PVD); preoperative atrial fibrillation (AF); left main disease (LMD); three vessel disease (TVD); left ventricle ejection fraction (LVEF) ≤49% and ≤30%, pre-operative use of intra-aortic balloon pump (IABP), non-elective admission, emergent/salvage operation, cardiogenic shock and year of operation. Overall risk profile was evaluated by using additive and logistic Euroscore. Incomplete revascularization (IR) was defined as at least one diseased primary arterial territory not grafted.

Short term outcomes investigated were postoperative complications including CVA, need for IABP defined as unplanned insertion of IABP intraoperatively or postoperatively due to hemodynamic instability or for weaning from cardiopulmonary bypass, re-exploration for bleeding, renal replacement therapy (RRT), sternal wound reconstruction as single and combined end-points and mortality within 30 days. Long term outcome was all-cause mortality. All-cause mortality is the most robust and unbiased index because no adjudication is required; thus, inaccurate or biased documentation or clinical assessments are avoided [15]. Information about death was obtained from the institutional database and the National General Register Office for

all patients. Data regarding postoperative complications and survival were available for all patients (100%) included.

Statistical analysis

For baseline characteristics, variables are summarized as mean for continuous variables and proportion for categorical variables. Multiple imputation using bootstrapping-based expectation-maximization algorithm and including all pre-treatment variables (Amelia R package, http://www.jstatsoft.org/v45/i07/) was used to address missing data (Supplementary Table 1 and Supplementary Figure 1). To control for measured potential confounders in the data set, a propensity score (PS) was generated for each patient from a multivariable logistic regression model based on pre-treatment covariates as independent variables with treatment type (OPCAB vs ONCAB) as a binary dependent variable [16]. The resulting propensity score represented the probability of a patient to undergo OPCAB (Area under the curve 0.63, Supplementary Figure 2). Pairs of patients receiving OPCAB and ONCAB were derived using greedy 1:1 matching with a calliper of width of 0.2 standard deviation of the logit of the PS (non-random R package, http://CRAN.Rproject.org/package=nonrandom). The quality of the match was assessed by comparing selected pre-treatment variables in propensity score–matched patient using the standardized mean difference (SMD), by which an absolute standardized difference of greater than 10% is suggested to represent meaningful covariate imbalance [16]. Analytic methods for the estimation of the treatment effect in the matched sample included McNemar's to compare proportions [16]. Time-segmented Cox regression models (within 30 days and beyond 30 days) [17] that stratified on the matched pairs [18] were used to investigate the effect of treatment (ONCAB vs ONCAB) on early and late mortality. This approach accounts for the

within-pair homogeneity by allowing the baseline hazard function to vary across matched sets (survival R package, http://CRAN.R-project.org/package=survival). Lastly a multivariate adjustment for all baseline characteristics and intraoperative variables such as the use of bilateral internal thoracic arteries (BITAs), the use of the Radial Artery (RA) and the incidence of incomplete revascularization was performed in the matched sample to correct the effect of OPCAB for residual imbalance (double robust) and to estimate the effect size of other covariates on all outcomes investigated. Person correlation coefficient and variance inflation factors (VIF) from the covariance matrix of parameter estimates was used to assess collinearity in multivariate models (usdm R package, http://CRAN.R-project.org/package=usdm). Variables with VIF higher than 4 were excluded from multivariate analyses. All p-values <0.05 were considered to indicate statistical significance. All statistical analysis was performed using R Statistical Software (version 3.2.3; R Foundation for Statistical Computing, Vienna, Austria).

Results

Pre-treatment variables distribution in OPCAB and ONCAB groups are summarized in Table 1. Patients undergoing ONCAB were likely to have CCS III/IV, three vessel disease, LVEF≤30% and cardiogenic shock. Era of surgery was also different between the two groups. Additive Euroscore (P=0.02) but not logistic Euroscore (P=0.15) was higher in the ONCAB group. PSM created a total of 995 pairs perfectly matched for all pre-treatment variables (SMD<0.10) including era of surgery. In the matched population additive Euroscore (P=0.08) and logistic Euroscore (P=0.12) were comparable between the two groups.

Intraoperative data

Table 2 summarizes intraoperative data. When compared to ONCAB, OPCAB was associated with a lower number of grafts per patient (2.7±0.7 versus 3.0±0.7 P<0.001; Figure 2) in all but left anterior descending artery territories. The rate of bilateral internal thoracic artery grafting was particular low in both groups (P=0.1). The use of the radial artery was higher in the OPCAB group while saphenous vein graft was more frequently used in the ONCAB group. OPCAB conversion rate was 7/1253 (0.6%).

Effect of OPCAB on short term outcomes

Short term outcomes are summarized in Table 3. OPCAB was associated with a higher rate of IR. However, when compared to ONCAB, OPCAB was significantly associated with 50% relative risk reduction for postoperative CVA (P=0.04), need for postoperative IABP (P=0.002) and re-exploration for bleeding (P=0.02). Overall mortality within 30 days was 2.4% (58 pts) without significant difference between the two groups. This trend toward a benefit from OPCAB on short term outcomes was confirmed when results were analysed separately for patients on oral treatment and on insulin (Supplementary Table 2 and 3). Among seven OPCAB cases which required conversion to ONCAB, no deaths within 30 days were recorded.

Effect of OPCAB on long term mortality

At a mean follow-up time of 6.5±4.5 years, there were 357 and 408 deaths in the unmatched population and 284 and 299 deaths in the matched sample in the OPCAB and ONCAB groups respectively (Figure 2). In the matched sample survival probability at 5 and 10 was 82.6±1.2% and 62.6±2.0% and versus 84.3±1.3% and 64.0±1.9% in the OPCAB and ONCAB group respectively. The two strategies were perfectly comparable in terms of late mortality in the overall matched sample (HR 1.08;95%CI 0.92-1.28; P=0.32) and among patients orally treated (HR 1.06;95%CI0.85-1.33; P=0.6) and on insulin (HR 1.12; 95%CI 0.88-1.43; P=0.35, Figure 3).

OPCAB with complete revascularization showed comparable survival when compared to ONCAB with complete revascularization (n=921) (HR 1.00; 95%CI 0.84-1.20; P=0.96). OPCAB patients with IR (n=139) showed reduced survival rate when compared to OPCAB with complete revascularization (n=856) (HR 1.82; 95%CI 1.34-2.46; P=0.0002) and ONCAB with complete revascularization (HR 1.83; 95%CI1.36-2.47; P<0.0001; Figure 4). We could not draw conclusion on the impact on IR among ONCAB subjects due to their small sample size (n=74).

Effect of OPCAB over ONCAB after full adjustment (double robust)

After double robust adjustment. OPCAB was confirmed to be significantly associated with a reduced incidence of postoperative stroke, need for postoperative IABP, sternal wound reconstruction, re-exploration for bleeding but not dialysis. OPACB was significantly associated with a 2-fold increased risk of incomplete revascularization. OPACB was not associated with increased early (within 30 days) and late mortality (Supplementary Table 4, central picture).

Impact of other predictors of outcomes

Impact of other predictors on outcomes of interest is reported in Supplementary Tables 5 to 13. In particular, diabetes on insulin was significantly associated with increased risk of postoperative dialysis and incidence of any complication. Diabetes on insulin did not significantly affect early mortality but was associated with 18% relative risk increase in late mortality. IR did not significantly influence operative outcomes and early mortality. However, it was associated with nearly 50% relative risk increase in late mortality. All variables investigated showed VIF < 4 (Supplementary Table 14).

Discussion

To the best of our knowledge this is the largest series with the longest follow-up on the impact of OPCAB in patients with actively treated diabetes with multivessel coronary

disease. We found that OPCAB was associated with a trend towards a lower incidence of postoperative complications including postoperative cardiovascular accidents. OPCAB showed comparable early and late survival when compared to ONCAB. The present analysis confirmed that OPCAB was associated with a ~7% absolute risk increase in incomplete revascularization and OPCAB with IR showed a lower survival rate when compared to OPCAB and ONCAB with complete revascularization. Insulin treatment was confirmed to be an independent risk factor for postoperative complications in particular need for renal replacement therapy and was associated with poorer long term survival.

Despite several randomized controlled trials there is still controversy with respect to the advantages and disadvantages of OPCAB vs OPCAB surgery [7-9,19,20], However, some evidence has suggested a potential off-pump benefit for high operative risk patient subgroups [21-23]. In the case of diabetic patients with multivessel disease only limited data are available with conflicting reports [10-13]. A recent observational sub-analysis of the BARI 2D trial [10] concluded that patients with diabetes had greater risk of major long-term cardiovascular events after OPCAB than after ONCAB. However, this study has been criticized [14] due to the small number of patients compared (153 propensity matched pairs) which is inadequate to draw final conclusions. Moreover there was missing information regarding the completeness of revascularization. A sub-analysis of the ROOBY trial [11] on diabetic patients randomized to OPCAB (n=402) or ONCAB (n=433) concluded that 1-year graft patency rate was lower after OPCAB with no difference in the 1-year primary composite outcome. However, it is largely recognized that in the ROOBY Trial, surgeons were inexperienced (on average performing eight OPCAB operations per year and with a high conversion rate of around 12% [14]. The importance of surgeon

experience in OPCAB is clearly demonstrated in trials that showed no difference in hard clinical end-points at 1 year or at longer follow up [7,8,24]. Moreover, the 1% lower graft patency rate reported in the OPCAB group is clearly marginal (83.1% vs 88.4%) and it is likely not to have any clinical impact. On the other hand, Emmert et al. [12] compared short term outcomes in 540 OPCAB and 475 ONCAB diabetic patients, and showed a clear trend to reduced major complications such as stroke, re-thoracotomy for bleeding, and postoperative IABP requirement, confirming the beneficial effect of OPCAB on short term outcomes in this subset of patients. Renner et al. [13] compared 355 OPCAB and 502 ONCAB procedure and they concluded that OPCAB was associated with a significant lower 30-day mortality risk and also with a lower 1 year mortality risk compared with ONCAB.

In the present analysis, IR occurred in 15.2% and 7.9% of unmatched OPCAB and ONCAB groups respectively. Although patients undergoing OPCAB with complete revascularization showed survival rates similar to those receiving ONCAB, OPCAB with IR was found to be significantly associated with a lower survival rate when compared to OPCAB and ONCAB with complete revascularization. It has been suggested that patients who undergo IR have multiple comorbidities and unfavorable anatomy that could bias the data in favour of complete revascularization [25]. However compelling evidence supports the hypothesis that diabetics are more likely to benefit from a more complete revascularization [26]. Raza et al. recently reported a long term survival analysis on 11922 diabetic patients [27] and they demonstrated that complete revascularization was associated with 10% lower late mortality. Moreover, they found that OPCAB was associated with 10% lower late mortality than ONCAB, but the difference was not statistically significant ($P = 0.2$). Nakano et al. [28] reported on 604 consecutive patients underwent OPCAB during a 6-year period. A total of 216 patients

had IR (13%), They found that all the event-free survival rates for all-cause mortality (P < .001), cardiac death (P = .020), and major adverse cardiac and cerebrovascular events (P < .001) were lower in the IR group. Of note, IR rate observed in the present OPCAB series was significantly lower than that reported by others. Omer at al. [29] recently reported a 29% rate of IR in 6367 OPCAB cases compared to 11.0% in 34,772 ONCAB cases. Kleisli et al. [30] reported a 22% rate of IR in 207 OPCAB and 6.3% in 827 ONCAB patients. Some have suggested that surgeon experience plays a role and emphasized the importance of surgeon volume in establishing favorable outcomes for OPCAB [24].The relatively low rate of IR in the present OPCAB series might partially related to the high OPCAB volume in our centre and support the hypothesis that when OPCAB is routinely performed, complete revascularization can be achieved in the majority of cases. Considering that the trend toward shorter survival with OPCAB observed in some studies may be related to incomplete revascularization [27,28], which seems more likely with less experienced surgeons with the technique, it is prudent to consider that OPCAB is not a surgery that should be performed routinely by any cardiac surgeon, but due to its beneficial potential in specific situations and in particular among diabetics, every surgeon should enable himself to perform it through proper training and use of specific available technology. Finally, although the use of additional grafts has been shown to minimize the risk related to incomplete revascularization [31], in the present series the rate of bilateral internal thoracic arteries usage has been particularly low (~2%) and this is partially due to the perceived increased vulnerability to sternal wound complication in this high risk cases [27].

Limitations

The main limitation of our study is that no follow-up data were available to compare the groups with respect to the cause of death (cardiac vs noncardiac), recurrence of

angina, need for repeated revascularization, and graft patency. Therefore, we can only speculate about the mechanism beyond the equipoise between OPCAB and ONCAB on long-term survival. Finally, although the data were collected prospectively, the nonspecific design of the data for the analysis of the diabetic population limits the present analysis. Propensity technique can adjust only for measurable and included variables and we cannot exclude a selection bias based on non-measurable “eye-ball”.

In conclusion, OPCAB is a safe and feasible option for diabetic patients with multivessel coronary disease. OPCAB reduces the incidence of postoperative complications and provides long term survival comparable to ONCAB strategy. Complete revascularization should still be the main goal while performing OPCAB surgery in diabetics.

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1 Table 1. Pre-treatment variables distribution in the unmatched and matched OPCAB and ONCAB groups

		Unmatched OPCAB		Unmatched OPCAB		SMD	PS-matched OPCAB		PS-matched OPCAB		SMD
		n	%	n	%		n	%	n	%	
Total sample		1253	100.0	1197	100.0		995	100.0	995	100.0	
Age	<60.0	307	24.5	282	23.6	4.8	242	24.3	233	23.4	2.4
	60-69	449	35.8	490	40.9		360	36.2	393	39.5	
	70-79	440	35.1	401	33.5		346	34.8	345	34.7	
	≥8	57	4.5	24	2.0		47	4.7	24	2.4	
Female	No	976	77.9	929	77.6	0.7	765	76.9	762	76.6	0.7
	Yes	277	22.1	268	22.4		230	23.1	233	23.4	
BMI	<30	723	57.7	726	60.7	7.5	575	57.8	575	57.8	1.1
	≥30	530	42.3	471	39.3		420	42.2	420	42.2	
CCS	No	654	52.2	526	43.9	16.5	514	51.7	491	49.3	4.6
	Yes	599	47.8	671	56.1		481	48.3	504	50.7	
NYHA	No	791	63.1	704	58.8	8.8	624	62.7	611	61.4	2.7
	Yes	462	36.9	493	41.2		371	37.3	384	38.6	
MI within 30 days	No	985	78.6	932	77.9	1.8	796	80.0	768	77.2	6.8
	Yes	268	21.4	265	22.1		199	20.0	227	22.8	
PCI	No	1157	92.3	1125	94.0	6.5	917	92.2	925	93.0	3.0
	Yes	96	7.7	72	6.0		78	7.8	70	7.0	
DM on insulin	No	733	58.5	706	59.0	0.9	583	58.6	584	58.7	0.2

	Yes	520	41.5	491	41.0		412	41.4	411	41.3	
Current smoking	No	1117	89.1	1060	88.6	1.8	889	89.3	888	89.2	0.3
	Yes	136	10.9	137	11.4		106	10.7	107	10.8	
sCr>200mmol/l	No	1204	96.1	1147	95.8	1.3	956	96.1	958	96.3	1.0
	Yes	49	3.9	50	4.2		39	3.9	37	3.7	
COPD	No	1140	91.0	1086	90.7	0.8	903	90.8	899	90.4	1.3
	Yes	113	9.0	111	9.3		92	9.2	96	9.6	
CVA	No	1179	94.1	1131	94.5	1.6	931	93.6	940	94.5	3.8
	Yes	74	5.9	66	5.5		64	6.4	55	5.5	
PVD	No	1075	85.8	991	82.8	8.2	853	85.7	848	85.2	1.4
	Yes	178	14.2	206	17.2		142	14.3	147	14.8	
AF	No	1198	95.6	1142	95.4	0.9	949	95.4	951	95.6	0.9
	Yes	55	4.4	55	4.6		46	4.6	44	4.4	
TVD	No	346	27.6	230	19.2	19.9	298	29.9	224	22.5	9.2
	Yes	907	72.4	967	80.8		697	70.1	771	77.5	
LMD	No	964	76.9	913	76.3	1.5	770	77.4	753	75.7	4.0
	Yes	289	23.1	284	23.7		225	22.6	242	24.3	
LVEF<50%	No	839	67.0	786	65.7	2.7	660	66.3	663	66.6	0.6
	Yes	414	33.0	411	34.3		335	33.7	332	33.4	
LVEF 30-49%	No	923	73.7	902	75.4	2.7	729	73.3	737	74.1	
	Yes	330	26.3	295	24.6		266	26.7	258	25.9	

LVEF<30%	No	1169	93.3	1081	90.3	10.9	926	93.1	921	92.6	1.9
	Yes	84	6.7	116	9.7		69	6.9	74	7.4	
Cardiogenic shock	No	1247	99.5	1178	98.4	10.9	990	99.5	990	99.5	0.0
	Yes	6	0.5	19	1.6		5	0.5	5	0.5	
preop IABP	No	1237	98.7	1167	97.5	9.0	981	98.6	981	98.6	0.3
	Yes	16	1.3	30	2.5		14	1.4	14	1.4	
non elective	No	644	51.4	560	46.8	9.2	520	52.3	476	47.8	8.8
	Yes	609	48.6	637	53.2		475	47.7	519	52.2	
Emergent/salvage	No	1239	98.9	1171	97.8	8.3	982	98.7	980	98.5	1.7
	Yes	14	1.1	26	2.2		13	1.3	15	1.5	
Era of surgery	1996-2004	398	31.8	306	25.6	34.6	254	25.5	256	25.7	9.8
	2005-2007	267	21.3	349	29.2		273	27.4	276	27.7	
	2008-2010	324	25.9	283	23.6		240	24.1	269	27.0	
	2011-2015	264	21.1	259	21.6		228	22.9	194	19.5	
AdditiveEuroscore		4.2±2.6		4.4±2.8			4.2±2.7		4.2±2.5		
Logistic Euroscore		5±5%		5±7%			5±5%		4±5%		

OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass; PS: propensity score; SMD: standardised mean difference; BMI: body mass index; CCS: Canadian cardiovascular class; NYHA: New York Heart Association; MI: myocardial

infarction; PCI: percutaneous coronary intervention; DM diabetes mellitus; sCr: serum creatinine; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; PVD: peripheral vascular disease; AF: atrial fibrillation; TVD: 3-vessel disease; LMD: left main disease; LVEF: left ventricular ejection fraction; IABP: intra-aortic balloon pump.

Table 2. Intraoperative data

		OPCAB		ONCAB		P value
		n	%	n	%	
Overall		1253	100.0	1197	100.0	
Number of grafts	1	36	2.9	6	0.5	<0.001
	2	447	35.7	253	21.1	
	3	650	51.9	703	58.7	
	4	119	9.5	222	18.5	
	5	1	0.1	12	1.0	
	6	0	0.0	1	0.1	
Mean number of grafts/pt		2.7±0.7		3.0±0.7		
Graft target						
LAD	No	35	2.8	33	2.8	1
	Yes	1218	97.2	1164	97.2	
DIA	No	1020	81.4	931	77.8	0.03
	Yes	233	18.6	266	22.2	
CX	No	313	25.0	142	11.9	<0.001
	Yes	940	75.0	1055	88.1	
RCA	No	398	31.8	305	25.5	<0.001
	Yes	855	68.2	892	74.5	
RITA	No	1224	97.7	1160	96.9	0.3
	Yes	29	2.3	37	3.1	
LITA	No	76	6.1	113	9.4	0.002
	Yes	1177	93.9	1084	90.6	
BITA	No	1230	98.2	1163	97.2	0.1

	Yes	23	1.8	34	2.8	
RA	No	986	78.7	1083	90.5	<0.001
	Yes	267	21.3	114	9.5	
SV	No	137	10.9	58	4.8	<0.001
	Yes	1116	89.1	1139	95.2	
sequential grafts	No	1154	92.1	1150	96.1	<0.001
	Yes	99	7.9	47	3.9	

LAD: left anterior descending artery; DIA: diagonal branch; CX: circumflex artery; RCA: right coronary artery; LITA: left interior thoracic artery; RITA: right interior thoracic artery; BITA: bilateral internal thoracic artery; RA: radial artery; SV: saphenous vein

Table 3. Short term outcomes in the unmatched and matched OPCAB and ONCAB groups with relative effect size in the propensity score-matched population. (OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass; PS: propensity score; CVA: cerebrovascular event; RRT: renal replacement therapy; SWR: sternal wound reconstruction; IABP intra-aortic balloon pump)

		unmatched OPCAB		unmatched ONCAB		PS-matched OPCAB		PS-matched ONCAB		PSM-adjusted estimate [95%CI]	adjusted P
		n	%	n	%	n	%	n	%		
Sample size		1253	100.0	1197	100.0	995	100.0	995	100.0		
CVA	No	1235	98.6	1167	97.5	983	98.8	971	97.6	0.49[0.25-0.99]	0.04
	Yes	18	1.4	30	2.5	12	1.2	24	2.4		
RRT	No	1193	95.2	1144	95.6	946	95.1	952	95.7	1.15[0.75-1.74]	0.52
	Yes	60	4.8	53	4.4	49	4.9	43	4.3		
IABP	No	1221	97.4	1136	94.9	969	97.4	942	94.7	0.48[0.30-0.77]	0.002
	Yes	32	2.6	61	5.1	26	2.6	53	5.3		
SWR	No	1240	99.0	1180	98.6	985	99.0	979	98.4	0.62[0.28-1.38]	0.24
	Yes	13	1.0	17	1.4	10	1.0	16	1.6		
Re-exploration	No	1224	97.7	1155	96.5	973	97.8	956	96.1	0.55[0.33-0.94]	0.02
	Yes	29	2.3	42	3.5	22	2.2	39	3.9		
Any complication	No	1118	89.2	1028	85.9	890	89.4	849	85.3	0.69[0.52-0.90]	0.005
	Yes	135	10.8	169	14.1	105	10.6	146	14.7		

30-day mortality	No	1221	97.4	1171	97.8	970	97.5	976	98.1	1.32[0.73-2.40]	0.36
	Yes	32	2.6	26	2.2	25	2.5	19	1.9		
IR	No	1062	84.8	1102	92.1	865	86.9	921	92.6	2[1.50-2.7]	<0.001
	Yes	191	15.2	95	7.9	139	14.0	74	7.4		

OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass; PS: propensity score; CVA: cerebrovascular event; RRT: renal replacement therapy; SWR: sternal wound reconstruction; IABP intra-aortic balloon pump

Supplementary Table 1. Percentage of missing data

preoperative IABP	19.776	COPD	0.635
sCr	19.518	CCS	0.622
BMI	10.424	AF	0.622
LMD	7.494	DMI	0.615
MI30d	7.322	PCI	0.463
TVD	1.984	shock	0.417
CVA	1.508	non elective	0.093
LVEF	1.27	emergent/salvage	0.093
Current smoking	0.701	Age	0
NYHA	0.688	Female	0
PVD	0.661	Era of surgery	0

BMI: body mass index; CCS: Canadian cardiovascular class; NYHA: New York Heart Association; MI: myocardial infarction; PCI: percutaneous coronary intervention; DM diabetes mellitus; sCr: serum creatinine; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; PVD: peripheral vascular disease; AF: atrial fibrillation; TVD: 3-vessel disease; LMD: left main disease; LVEF: left ventricular ejection fraction; IABP: intra-aortic balloon pump.

Supplementary Table 2. Short term outcomes in patients with orally treated diabetes in the unmatched and matched OPCAB and ONCAB groups with relative effect size in the propensity score-matched population.

		unmatched OPCAB		unmatched ONCAB		PS-matched OPCAB		PS-matched ONCAB		adjusted estimate [95%CI]	adjusted P
		n	%	n	%	n	%	n	%		
Sample size		733	100.0	706	100.0	583	100.0	584	100.0		
CVA	No	724	98.8	685	97.0	578	99.1	568	97.3	0.31[0.11-0.84]	0.02
	Yes	9	1.2	21	3.0	5	0.9	16	2.7		
RRT	No	706	96.3	683	96.7	562	96.4	565	96.7	1.11[0.592.09]	0.74
	Yes	27	3.7	23	3.3	21	3.6	19	3.3		
IABP	No	714	97.4	672	95.2	569	97.6	555	95.0	0.47[0.25-0.90]	0.02
	Yes	19	2.6	34	4.8	14	2.4	29	5.0		
SWR	No	728	99.3	696	98.6	579	99.3	575	98.5	0.44[0.14-1.44]	0.17
	Yes	5	0.7	10	1.4	4	0.7	9	1.5		
Re-exploration	No	717	97.8	681	96.5	570	97.8	560	95.9	0.53[0.27-1.05]	0.07
	Yes	16	2.2	25	3.5	13	2.2	24	4.1		
Any complication	No	663	90.5	614	87.0	531	91.1	505	86.5	0.63[0.43-0.90]	0.01
	Yes	70	9.5	92	13.0	52	8.9	79	13.5		
30-day mortality	No	717	97.8	691	97.9	573	98.3	573	98.1	0.89[0.38-2.09]	0.78
	Yes	16	2.2	15	2.1	10	1.7	11	1.9		

IR	No	621	84.7	653	92.5	499	85.6	543	93.0	2.2[1.51-3.3]	<0.001
	Yes	112	15.3	53	7.5	84	14.4	41	7.0		

OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass; PS: propensity score; CVA: cerebrovascular event; RRT: renal replacement therapy; SWR: sternal wound reconstruction; IABP intra-aortic balloon pump

Supplementary Table 3. Short term outcomes in patients on insulin in the unmatched and matched OPCAB and ONCAB groups with relative effect size in the propensity score-matched population. (OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass; PS: propensity score; CVA: cerebrovascular event; RRT: renal replacement therapy; SWR: sternal wound reconstruction; IABP intra-aortic balloon pump)

		unmatched OPCAB		unmatched ONCAB		PS-matched OPCAB		PS-matched ONCAB		adjusted estimate [95%CI]	adjusted P
		n	%	n	%	n	%	n	%		
Sample size		520	100.0	491	100	412	100.0	411	100.0		
CVA	No	511	98.3	482	98	405	98.3	403	98.1	0.87[0.31-2.42]	0.79
	Yes	9	1.7	9	2	7	1.7	8	1.9		
RRT	No	487	93.7	461	94	384	93.2	387	94.2	1.18[0.67-2.06]	0.57
	Yes	33	6.3	30	6	28	6.8	24	5.8		
IABP	No	507	97.5	464	95	400	97.1	387	94.2	0.48[0.24-0.98]	0.04
	Yes	13	2.5	27	5	12	2.9	24	5.8		
SWR	No	512	98.5	484	99	406	98.5	404	98.3	0.85[0.28-2.56]	0.77
	Yes	8	1.5	7	1	6	1.5	7	1.7		
Re-exploration	No	507	97.5	474	97	403	97.8	396	96.4	0.59[0.26-1.36]	0.21
	Yes	13	2.5	17	3	9	2.2	15	3.6		
Any complication	No	455	87.5	414	84	359	87.1	344	83.7	0.77[0.54-0.99]	0.04
	Yes	65	12.5	77	16	53	12.9	67	16.3		

30-day mortality	No	504	96.9	480	98	397	96.4	403	98.1	1.81[0.77-4.28]	0.19
	Yes	16	3.1	11	2	15	3.6	8	1.9		
IR	No	441	84.8	449	91	357	86.7	378	92.0	1.76[1.12-2.8]	0.01
	Yes	79	15.2	42	9	55	13.3	33	8.0		

OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass; PS: propensity score; CVA: cerebrovascular event; RRT: renal replacement therapy; SWR: sternal wound reconstruction; IABP intra-aortic balloon pump

Supplementary Table 4. Effect of off-pump coronary artery bypass (OPCAB) grafting over on-pump coronary artery bypass (ONCAB) grafting on outcomes of interest in a fully adjusted double robust analyisis.

	Effect size	lower 95%CI	upper 95%CI	P
Postoperative CVA	0.47*	0.23	0.97	0.04
Postoperative RRT	1.23*	0.77	1.97	0.55
Sternal wound reconstruction	0.35*	0.14	0.88	0.04
Re-exploration for bleeding	0.57*	0.33	0.99	0.04
Postoperative IABP	0.49*	0.3	0.82	0.009
Any of above complication	0.7*	0.51	0.95	0.02
Mortality at 30 days	1.4$^{\mp}$	0.75	2.61	0.19
Incomplete revascularization	2.41*	1.75	3.32	<0.0001
Late mortality	1.09 $^{\mp}$	0.91	1.29	0.55

*Logistic regression model; $^{\mp}$ Cox regression model; CI: confidence interval

CVA: cerebrovascular event; RRT: renal replacement therapy; IABP: intra-aortic balloon pump.

Supplementary Table 5. Double robust analysis on postoperative cerebrovascular accident.

	Effect	Lower 0.95CI	Upper 0.95CI
OPCAB	0.47	0.23	0.97
Age	1.25	0.71	2.18
Female	1.17	0.51	2.67
Body mass index	1.43	0.82	2.51
Canadian Cardiovascular Class	0.7	0.32	1.5
New Your Heart Association Class	1.29	0.59	2.8
Myocardial Infarction within 30 day	0.81	0.33	1.97
Percutaneous Coronary intervention	1.26	0.39	4.01
Diabetes Mellitus on insulin	1.03	0.5	2.11
Current smoking	1.44	0.5	4.16
Creatinine > 200 mmol/l	2.3	0.62	8.48
Chronic Obstructive Pulmonary Disease	0.33	0.07	1.52
Cerebrovascular accident	4.16	1.67	10.36
Peripheral vascular disease	2.1	0.94	4.68
Atrial fibrillation	0.65	0.08	5.02
3-vessel disease	1.37	0.57	3.32
Left main disease	1.61	0.75	3.43
Left ventricular ejection fraction 30%-49%	0.62	0.27	1.46
Left ventricular ejection fraction <30%	0.49	0.1	2.53
Cardiogenic shock	4.5	0.26	76.93
preop intraaortic balloon pump	2.75	0.47	16.09
non elective	1.57	0.71	3.49
emergent/salvage	2.76	0.4	18.91
Era of surgery	1.81	1	3.28
Bilateral internal thoracic arteries	2.21	0.26	18.59

Radial artery	0.8	0.23	2.83
Incomplete revascularization	1.01	0.33	3.06

Supplementary Table 6. Double robust analysis on postoperative renal replacement therapy.

	Effect	Lower 0.95CI	Upper 0.95CI
OPCAB	1.23	0.77	1.97
Age	1.22	0.86	1.74
Female	0.76	0.43	1.34
Body mass index	1.27	0.92	1.74
Canadian Cardiovascular Class	1.25	0.78	2.01
New Your Heart Association Class	0.73	0.45	1.21
Myocardial Infarction within 30 day	0.66	0.36	1.2
Percutaneous Coronary intervention	0.74	0.32	1.72
Diabetes Mellitus on insulin	1.91	1.22	3
Current smoking	0.98	0.45	2.11
Creatinine > 200 mmol/l	5.24	2.65	10.35
Chronic Obstructive Pulmonary Disease	0.66	0.31	1.41
Cerebrovascular accident	2.11	1.04	4.27
Peripheral vascular disease	1.47	0.85	2.53
Atrial fibrillation	1.92	0.82	4.49
3-vessel disease	0.89	0.53	1.48
Left main disease	1.44	0.88	2.37
Left ventricular ejection fraction 30%-49%	0.94	0.56	1.57
Left ventricular ejection fraction <30%	1.26	0.56	2.86
Cardiogenic shock	4.26	0.57	31.57
preop intraaortic balloon pump	3.68	1.08	12.56
non elective	1.05	0.64	1.72
emergent/salvage	1.16	0.18	7.38
Era of surgery	1.95	1.29	2.94
Bilateral internal thoracic arteries	0.94	0.12	7.34
Radial artery	0.76	0.36	1.61
Incomplete revascularization	0.75	0.35	1.59

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50 Supplementary Table 7. Double robust analysis on need for intra-aortic balloon pump.

	Effect	Lower 0.95CI	Upper 0.95CI
OPCAB	0.49	0.3	0.82
Age	0.97	0.65	1.43
Female	1.27	0.72	2.24
Body mass index	0.82	0.6	1.11
Canadian Cardiovascular Class	1.22	0.7	2.12
New Your Heart Association Class	1.29	0.74	2.25
Myocardial Infarction within 30 day	1.68	0.91	3.1
Percutaneous Coronary intervention	0.78	0.31	1.97
Diabetes Mellitus on insulin	1.18	0.71	1.96
Current smoking	0.24	0.07	0.84
Creatinine > 200 mmol/l	2.5	1.03	6.09
Chronic Obstructive Pulmonary Disease	0.65	0.26	1.66
Cerebrovascular accident	0.3	0.04	2.24
Peripheral vascular disease	0.77	0.38	1.55
Atrial fibrillation	1.74	0.65	4.66
3-vessel disease	0.91	0.5	1.65
Left main disease	1.31	0.75	2.29
Left ventricular ejection fraction 30%-49%	2.09	1.17	3.76
Left ventricular ejection fraction <30%	8.3	4.32	15.93
Cardiogenic shock	1.44	0.15	13.66
preop intraaortic balloon pump	0.14	0.01	2.4
non elective	0.87	0.48	1.57
emergent/salvage	6.34	2.08	19.29

Era of surgery	1.75	1.15	2.66
Bilateral internal thoracic arteries	3.58	0.89	14.33
Radial artery	0.36	0.11	1.2
Incomplete revascularization	0.92	0.42	2.03

51 Supplementary Table 8. Double robust analysis on risk of sternal wound reconstruction.

	Effect	Lower 0.95CI	Upper 0.95CI
OPCAB	0.35	0.14	0.88
Age	2.52	1.19	5.34
Female	0.52	0.15	1.84
Body mass index	2.23	0.97	5.11
Canadian Cardiovascular Class	1.07	0.44	2.59
New Your Heart Association Class	0.39	0.15	1.04
Myocardial Infarction within 30 day	0.43	0.13	1.43
Percutaneous Coronary intervention	2.06	0.67	6.33
Diabetes Mellitus on insulin	1.53	0.65	3.6
Current smoking	0.81	0.16	3.97
Creatinine > 200 mmol/l	4.56	1.26	16.52
Chronic Obstructive Pulmonary Disease	3.62	1.4	9.39
Cerebrovascular accident	0.68	0.08	5.56
Peripheral vascular disease	0.61	0.17	2.18
Atrial fibrillation	1.25	0.27	5.8
3-vessel disease	0.33	0.13	1.01
Left main disease	1.12	0.44	2.87
Left ventricular ejection fraction 30%-49%	2.08	0.84	5.13
Left ventricular ejection fraction <30%	2.95	0.75	11.67
Cardiogenic shock	-	-	-
preop intraaortic balloon pump	-	-	-
non elective	1.3	0.51	3.34
emergent/salvage	-	-	-
Era of surgery	2	0.7	5.72

Bilateral internal thoracic arteries	-	-	-
Radial artery	2.07	0.62	6.93
Incomplete revascularization	1.01	0.21	4.92

Supplementary Table 9. Double robust analysis on risk of re-exploration for bleeding.

	Effect	Lower 0.95CI	Upper 0.95CI
OPCAB	0.57	0.33	0.99
Age	0.98	0.64	1.5
Female	1.1	0.59	2.06
Body mass index	0.91	0.64	1.31
Canadian Cardiovascular Class	1.35	0.74	2.44
New Your Heart Association Class	0.55	0.29	1.03
Myocardial Infarction within 30 day	1.37	0.71	2.65
Percutaneous Coronary intervention	0.33	0.08	1.44
Diabetes Mellitus on insulin	0.93	0.53	1.64
Current smoking	0.68	0.25	1.84
Creatinine > 200 mmol/l	2.77	1.03	7.47
Chronic Obstructive Pulmonary Disease	1.39	0.59	3.29
Cerebrovascular accident	0.54	0.13	2.3
Peripheral vascular disease	0.72	0.32	1.65
Atrial fibrillation	2.18	0.8	5.94
3-vessel disease	1.11	0.58	2.13
Left main disease	0.7	0.37	1.33
Left ventricular ejection fraction 30%-49%	0.72	0.37	1.4
Left ventricular ejection fraction <30%	1.66	0.71	3.9
Cardiogenic shock	13.13	1.66	104.09
preop intraaortic balloon pump	-	-	-
non elective	2.54	1.31	4.93
emergent/salvage	4.85	1.21	19.39
Era of surgery	1.08	0.67	1.75
Bilateral internal thoracic arteries	1.81	0.37	8.83
Radial artery	0.36	0.11	1.2
Incomplete revascularization	0.85	0.33	2.14

Supplementary Table 10. Double robust analysis on incidence of any complication among cerebrovascular accident, renal replacement therapy, need for intraaortic balloon pump, sternal wound reconstruction and re-exploration for bleeding.

	Effect	Lower 0.95CI	Upper 0.95CI
OPCAB	0.7	0.51	0.95
Age	1.03	1.01	1.05
Female	0.82	0.56	1.20
Body mass index	1.03	1	1.06
Diabetes mellitus on insulin	1.43	1.05	1.96
Canadian Cardiovascular Class	1.08	0.77	1.50
New Your Heart Association Class	0.84	0.6	1.19
Myocardial Infarction within 30 day	1.06	0.72	1.54
Percutaneous Coronary intervention	1.11	0.64	1.85
Current smoking	0.77	0.42	1.31
Creatinine > 200 mmol/l	5.15	2.98	8.75
Chronic Obstructive Pulmonary Disease	0.85	0.5	1.38
Cerebrovascular accident	1.65	0.92	2.81
Peripheral vascular disease	1.11	0.73	1.64
Atrial fibrillation	1.27	0.63	2.34
3-vessel disease	0.75	0.52	1.08
Left main disease	1.47	1.05	2.06
Left ventricular ejection fraction 30%-49%	1.3	0.91	1.83
Left ventricular ejection fraction <30%	3.04	1.85	4.90
Cardiogenic shock	0.85	0.13	4.38
preop intraaortic balloon pump	1.43	0.44	3.88
non elective	1.07	0.75	1.52
emergent/salvage	4.72	1.8	11.81
Era of surgery	1.65	1.14	2.41
Bilateral internal thoracic arteries	1.27	0.72	2.37
Radial artery	0.71	0.41	1.18

Incomplete revascularization	1.05	0.62	1.71

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59 Supplementary Table 11. Double robust analysis on mortality within 30 days

	Effect	Lower 0.95CI	Upper 0.95CI
OPCAB	1.4	0.75	2.61
Age	1.05	1.005	1.09
Female	1.64	0.86	3.14
Body mass index	0.81	0.55	1.2
Canadian Cardiovascular Class	1.65	0.81	3.36
New Your Heart Association Class	1.17	0.59	2.29
Myocardial Infarction within 30 day	1.01	0.48	2.13
Percutaneous Coronary intervention	1.49	0.49	4.54
Diabetes Mellitus on insulin	1.49	0.79	2.8
Current smoking	0.24	0.03	1.78
Creatinine > 200 mmol/l	1.03	0.23	4.54
Chronic Obstructive Pulmonary Disease	0.59	0.17	1.99
Cerebrovascular accident	1.5	0.52	4.32
Peripheral vascular disease	1.54	0.74	3.18
Atrial fibrillation	2.16	0.83	5.66
3-vessel disease	1.39	0.62	3.14
Left main disease	0.83	0.42	1.66
Left ventricular ejection fraction 30%-49%	2.59	1.3	5.17
Left ventricular ejection fraction <30%	3.79	1.54	9.32
Cardiogenic shock	1.24	0.06	25.92
preop intraaortic balloon pump	0.54	0.03	10.61
non elective	2.25	1.04	4.86
emergent/salvage	1.55	0.27	9
Era of surgery	0.76	0.4	1.46

Bilateral internal thoracic arteries	4.01	0.49	33.02
Radial artery	0.35	0.08	1.51
Incomplete revascularization	0.79	0.3	2.11

Supplementary Table 12. Double robust analysis on incomplete revascularization.

	Effect	Lower 0.95	Upper 0.95
OPCAB	2.41	1.75	3.32
Age	1.17	0.92	1.49
Female	1.4	1	1.96
Body mass index	0.94	0.78	1.14
Canadian Cardiovascular Class	0.87	0.63	1.2
New Your Heart Association Class	1.18	0.85	1.65
Myocardial Infarction within 30 day	0.79	0.53	1.19
Percutaneous Coronary intervention	0.66	0.35	1.21
Diabetes Mellitus on insulin	0.99	0.73	1.35
Current smoking	0.87	0.52	1.46
Creatinine > 200 mmol/l	1.07	0.52	2.17
Chronic Obstructive Pulmonary Disease	1.16	0.72	1.86
Cerebrovascular accident	1.01	0.55	1.87
Peripheral vascular disease	1.01	0.67	1.53
Atrial fibrillation	0.95	0.48	1.91
3-vessel disease	1.21	0.86	1.71
Left main disease	1.19	0.85	1.67
Left ventricular ejection fraction 30%-49%	0.99	0.55	1.77
Left ventricular ejection fraction <30%	0.52	0.05	5.47
Cardiogenic shock	1.14	0.35	3.68
preop intraaortic balloon pump	1.18	0.84	1.64
non elective	1.4	0.43	4.54

emergent/salvage	1.48	1.13	1.93
Era of surgery	1.48	0.5	4.41
Bilateral internal thoracic arteries	0.21	0.13	0.35
Radial artery	0.56	0.33	0.91

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Supplementary Table 13. Double robust analysis on late mortality.

	Effect	Lower 0.95	Upper 0.95
OPCAB	1.09	0.91	1.29
Age	1.06	1.04	1.07
Female	0.92	0.76	1.12
Body mass index	1.13	1.01	1.27
Canadian Cardiovascular Class	1.02	0.84	1.23
New Your Heart Association Class	1.06	0.87	1.28
Myocardial Infarction within 30 day	0.72	0.54	0.95
Percutaneous Coronary intervention	1.02	0.66	1.59
Diabetes Mellitus on insulin	1.18	1	1.4
Current smoking	1.27	0.93	1.72
Creatinine > 200 mmol/l	2.5	1.68	3.72
Chronic Obstructive Pulmonary Disease	1.38	1.03	1.83
Cerebrovascular accident	1.8	1.34	2.42
Peripheral vascular disease	1.72	1.39	2.14
Atrial fibrillation	1.82	1.32	2.52
3-vessel disease	0.87	0.71	1.07
Left main disease	1.1	0.9	1.35
Left ventricular ejection fraction 30%-49%	1.31	1.08	1.59
Left ventricular ejection fraction <30%	2.28	1.71	3.03
Cardiogenic shock	0.48	0.09	2.44
preop intraaortic balloon pump	1.2	0.39	3.7
non elective	1.18	0.97	1.42
emergent/salvage	1.13	0.53	2.41
Era of surgery	0.91	0.66	1.23
Bilateral internal thoracic arteries	0.87	0.43	1.77
Radial artery	1.07	0.84	1.36
Incomplete revascularization	1.49	1.15	1.92

Supplementary Table 14. Person correlation coefficient and variance inflation factors (VIF) from the covariance matrix

Pearson correlation between predictors	OPCAB	0.01	-0.00	-0.02	-0.01	-0.03
	IR	0.05	0.05	-0.00	0.03	-0.00
	TVD	0.09	-0.04	-0.01	0.02	0.06
	Era of Surgery	0.16	-0.09	-0.15	-0.06	0.30
	BMI	-0.14	0.06	0.08	0.13	0.01
	emergent/ salvage	-0.02	0.01	0.11	0.12	0.11
	non elective	0.09	0.06	0.23	0.07	0.38
	IABP	0.00	-0.01	0.03	0.03	0.05
	Cardiogenic shock	0.04	0.04	0.03	0.05	0.08
	LVEF	0.04	-0.05	0.03	0.12	0.11
	LMD	0.09	0.00	0.03	-0.01	0.10
	AF	0.10	-0.02	-0.01	0.04	0.00
	PVD	0.03	0.01	0.02	0.08	-0.01
	CVA	0.04	-0.02	-0.01	0.02	-0.01
	COPD	0.07	-0.04	0.01	0.15	0.02
	sCr>200mmol/l	-0.02	-0.00	0.00	0.04	0.04
	Current smoking	-0.24	0.00	-0.02	-0.01	0.14
	DM on insulin	-0.16	0.08	0.03	0.08	0.02
	PCI	-0.02	0.03	0.03	0.03	0.07
	MI	0.01	0.02	0.04	-0.01	1.00
	NYHA	0.09	0.12	0.34	1.00	-0.01
	CCS	-0.00	0.15	1.00	0.34	0.04
	Female	0.01	1.00	0.15	0.12	0.02
	Age	1.00	0.01	-0.00	0.09	0.01
VIF		1.24	1.06	1.25	1.24	1.34
		Age	Female	CCS	NYHA	MI

0.02	0.00	-0.00	0.01	-0.01	0.02	-0.01	0.00
-0.02	-0.00	-0.01	0.02	0.03	0.00	0.01	0.00
-0.06	0.01	0.00	0.04	0.04	0.05	0.01	-0.02
0.19	-0.05	0.07	0.05	0.14	-0.00	0.04	-0.01
0.03	0.09	0.01	-0.03	0.06	-0.00	-0.01	0.03
0.08	-0.01	-0.03	-0.02	-0.02	-0.01	-0.01	-0.03
0.04	0.03	0.06	0.01	0.04	0.02	0.03	0.03
0.06	0.00	0.00	-0.02	0.01	0.01	-0.04	-0.03
0.03	-0.02	-0.02	0.02	-0.02	-0.02	-0.03	0.02
0.01	0.07	0.02	0.05	0.04	-0.01	0.06	0.09
0.01	-0.04	-0.01	-0.02	0.04	-0.02	0.03	0.01
-0.02	-0.02	-0.02	-0.03	0.03	0.03	0.01	1.00
-0.02	0.07	0.03	0.04	0.07	0.08	1.00	0.01
-0.02	0.04	0.02	0.01	0.03	1.00	0.08	0.03
0.04	0.02	0.08	0.08	1.00	0.03	0.07	0.03
0.05	0.09	0.02	1.00	0.08	0.01	0.04	-0.03
0.06	-0.00	1.00	0.02	0.08	0.02	0.03	-0.02
0.03	1.00	-0.00	0.09	0.02	0.04	0.07	-0.02
1.00	0.03	0.06	0.05	0.04	-0.02	-0.02	-0.02
0.07	0.02	0.14	0.04	0.02	-0.01	-0.01	0.00
0.03	0.08	-0.01	0.04	0.15	0.02	0.08	0.04
0.03	0.03	-0.02	0.00	0.01	-0.01	0.02	-0.01
0.03	0.08	0.00	-0.00	-0.04	-0.02	0.01	-0.02
-0.02	-0.16	-0.24	-0.02	0.07	0.04	0.03	0.10
1.06	1.07	1.12	1.03	1.07	1.02	1.03	1.03
PCI	DM on insulin	Current smoking	sCr>200 mmol/l	COPD	CVA	PVD	AF

-0.02	0.00	0.00	-0.00	-0.04	-0.01	-0.01	0.06
0.03	0.03	-0.00	0.01	0.02	0.01	0.01	0.06
0.06	0.09	-0.01	0.01	0.08	0.01	-0.02	0.02
0.09	-0.01	-0.00	0.11	0.06	0.00	0.15	1.00
0.00	-0.03	-0.04	-0.00	-0.03	0.00	1.00	0.15
0.06	0.08	0.29	0.17	0.12	1.00	0.00	0.00
0.23	0.13	0.04	0.03	1.00	0.12	-0.03	0.06
0.01	0.07	0.29	1.00	0.03	0.17	-0.00	0.11
0.03	0.09	1.00	0.29	0.04	0.29	-0.04	-0.00
0.04	1.00	0.09	0.07	0.13	0.08	-0.03	-0.01
1.00	0.04	0.03	0.01	0.23	0.06	0.00	0.09
0.01	0.09	0.02	-0.03	0.03	-0.03	0.03	-0.01
0.03	0.06	-0.03	-0.04	0.03	-0.01	-0.01	0.04
-0.02	-0.01	-0.02	0.01	0.02	-0.01	-0.00	-0.00
0.04	0.04	-0.02	0.01	0.04	-0.02	0.06	0.14
-0.02	0.05	0.02	-0.02	0.01	-0.02	-0.03	0.05
-0.01	0.02	-0.02	0.00	0.06	-0.03	0.01	0.07
-0.04	0.07	-0.02	0.00	0.03	-0.01	0.09	-0.05
0.01	0.01	0.03	0.06	0.04	0.08	0.03	0.19
0.10	0.11	0.08	0.05	0.38	0.11	0.01	0.30
-0.01	0.12	0.05	0.03	0.07	0.12	0.13	-0.06
0.03	0.03	0.03	0.03	0.23	0.11	0.08	-0.15
0.00	-0.05	0.04	-0.01	0.06	0.01	0.06	-0.09
0.09	0.04	0.04	0.00	0.09	-0.02	-0.14	0.16
1.08	1.08	1.19	1.13	1.33	1.15	1.11	1.34
LMD	LVEF	Cardiogenic Shock	IABP	non elective	emergent/salvage	BMI	Era of surgery

TVD	1.09	0.09	-0.04	-0.01	0.02	0.06	-0.06	0.01	0.00	0.04	0.04	0.05	0.01	-0.02	0.06	0.09	-0.01	0.01	0.08	0.01	-0.02	0.02	1.00	0.21	-0.08
IR	1.07	0.05	0.05	-0.00	0.03	-0.00	-0.02	-0.00	-0.01	0.02	0.03	0.00	0.01	0.00	0.03	0.03	-0.00	0.01	0.02	0.01	0.01	0.06	0.21	1.00	0.11
OPCAB	1.03	0.01	-0.00	-0.02	-0.01	-0.03	0.02	0.00	-0.00	0.01	-0.01	0.02	-0.01	0.00	-0.02	0.00	0.00	-0.00	-0.04	-0.01	-0.01	0.06	-0.08	0.11	1.00

OPCAB: off-pump coronary artery bypass; BMI: body mass index; CCS: Canadian cardiovascular class; NYHA: New York Heart Association; MI: myocardial infarction; PCI: percutaneous coronary intervention; DM diabetes mellitus; sCr: serum creatinine; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; PVD: peripheral vascular disease; AF: atrial fibrillation; TVD: 3-vessel disease; LMD: left main disease; LVEF: left ventricular ejection fraction; IABP: intra-aortic balloon pump.

Figure Legend

Figure 1. Number of off-pump coronary artery bypass (OPCAB) and on-pump coronary artery bypass (ONCAB) operations during the study period

Figure 2. Survival curves in the unmatched and matched off-pump coronary artery bypass (OPCAB) and on-pump coronary artery bypass (ONCAB) groups.

Figure 3. Survival curves in the matched off-pump coronary artery bypass (OPCAB) and on-pump coronary artery bypass (ONCAB) groups in patients with oral treatment and in patients on insulin

Figure 4. Survival curves in the matched off-pump coronary artery bypass (OPCAB) and on-pump coronary artery bypass (ONCAB) groups in patients with complete (CR) and incomplete revascularization (IR)

Central figure. Effect of off-pump coronary artery bypass (OPCAB) grafting over on-pump coronary artery bypass (ONCAB) grafting on outcomes of interest. (CVA: cerebrovascular event; RRT: renal replacement therapy; SW: sternal wound; IABP intra-aortic balloon pump)

Supplementary Figure 1. Missing data and combinations overview.

Supplementary Figure 2. Area under the curve (AUC) for propensity score.

Video 1. Off-pump coronary artery bypass grafting technique at Bristol Heart Institute.